UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte JACK STAPLETON, BRADLEY BRITIGAN, and LARRY SCHLESINGER

Appeal No. 2005-1797
Application No. 09/954,975

ON BRIEF[1]

Before ELLIS, ADAMS and GREEN, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 11-40, which are all the claims pending in the application.

Claims 11, 31, 32 and 35 are illustrative of the subject matter on appeal and are reproduced below:

11. A method of treating a human subject infected with human immunodeficiency virus (HIV) comprising administering to said subject an amount of a gallium composition effective to inhibit HIV replication.

31. A method of reducing virus shed from a human subject infected with human immunodeficiency virus (HIV) comprising administering to said

[1] Appellants waived their request for oral hearing. See Paper received September 12, 2005. Accordingly, we considered this appeal on Supplemental Brief.

subject an amount of a gallium composition effective to inhibit HIV replication.

32. A method of reducing virus burden in a human subject infected with human immunodeficiency virus (HIV) comprising administering to said subject an amount of a gallium composition effective to inhibit HIV replication.

35. A method of inhibiting development of acquired immunodeficiency syndrome in a human subject infected with human immunodeficiency virus (HIV) comprising administering to said subject an amount of a gallium composition effective to inhibit HIV replication.

The references relied upon by the examiner are:

Murrer et al. (Murrer)	5,093,134	Mar. 3, 1992
Collery et al. (Collery)	5,525,598	Jun. 11, 1996
Bernstein	5,883,088	Mar. 16, 1999

Narsimhan, "The effect of copper and gallium compounds on ribonucleotide reductase," Abstract and p. 99 (UMI Dissertation Services) (1993).

GROUNDS OF REJECTION

Claims 11-13 and 16-40 stand rejected under 35 U.S.C. § 103. As evidence of obviousness the examiner relies on the combination of Murrer, Narasimhan, and appellants' acknowledged prior art.

Claims 11-40 stand rejected under 35 U.S.C. § 103. As evidence of obviousness the examiner relies on the combination of Narasimhan, Collery, Bernstein, and appellants' acknowledged prior art.

We affirm the rejection of claims 11-40 under 35 U.S.C. § 103 over the combination of Narasimhan, Collery, Bernstein and appellants' acknowledged prior art. Having disposed of all claims on appeal, we do not reach the merits of

the rejection of claims 11-13 and 16-40 under 35 U.S.C. § 103 over the combination of Murrer, and Narasimhan.

CLAIM GROUPING

According to appellants (Supplemental Brief, page 12), "claims 31, 32 and 35 stand separately patentable over the cited references." Accordingly, claims 12-30, 33, 34 and 36-40 stand or fall together with claim 11. Claims 31, 32 and 35 stand or fall alone.

DISCUSSION

According to the examiner (Answer, page 4), the basis for the rejections is "set forth in prior Office Action, Paper No. 4/23/2003." According to the record, the Office Action dated April 23, 2003 is the Final Rejection.

Narasimhan, Collery and Bernstein:

Claim 11:

Claim 11 is drawn to a method of treating a human infected with HIV. The claimed method comprises a single step – administering an amount of a gallium composition effective to inhibit HIV replication. Appellants' specification (page 4), recognizes gallium nitrate and a gallium-hydroxypyrone complex as examples of a gallium composition.

According to the examiner (Final Rejection, page 4), Narashimhan "teach that gallium, for example gallium nitrate ... inhibit[s] ribonucleotide reductase...."

In this regard, the examiner points out (id.) that appellants acknowledge "that inhibition of ribonucleotide reductase inhibits HIV replication and that ribonucleotide reductase inhibitors potentiate the activity of dideoxynucleotides which are nucleoside reverse transcriptase inhibitors...."

The examiner also finds (id.), Collery "teach that gallium complexes are effective in treating HIV and that gallium nitrate inhibits reverse transcriptase found in retroviruses, such as HIV...." In addition, we note that Collery teaches (column 1, lines 33-38), "preclinical toxicology tests suggest that renal and hepatic damages might be expected with gallium nitrate ... [but,] gallium III, administered ... in the form of an aqueous formulation of $GaCl_3$ at the therapeutical dosages involves no renal toxicity...." In this regard, Collery teaches that gallium (III) complexes not only have antitumor activity, but antiviral activities as well. Collery, column 1, lines 39-40.

Based on this evidence[2] the examiner finds (Final Rejection, page 5), a person of ordinary skill in the art at the time the invention was made would have found the claimed method prima facie obvious in view of the combination of Narashimhan and Collery. In this regard, we note that "[t]he test for obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of

[2] We recognize that the examiner also relies on Bernstein (Final Rejection, page 5), to teach "that gallium complexes of hydroxypyrones exhibit increased oral availability and are also suitable for administration intravenously...." It appears that the examiner relies on Bernstein to reach the subject matter of e.g., claim 15 which depends from and further limits gallium composition of claim 11 to a gallium-hydroxypyrone complex. Since claims 12-30, 33, 34, and 36-40 stand for fall together with claim 11, we find it unnecessary to discuss the Bernstein reference for its teaching of a gallium-hydroxypyrone complex.

ordinary skill in the art presumed to be familiar with them." In re Rosselet, 347 F.2d 847, 851, 146 USPQ 183, 186 (CCPA 1965).

On this record the examiner has established that gallium compositions have anti-viral activities and are effective in inhibiting the reverse transcriptase activity of retroviruses such as HIV. By inhibiting reverse transcriptase activity, HIV replication is inhibited. Collery teaches the use of gallium compositions as antiviral agents. See e.g., Collery, column 1, lines 6-8. Accordingly, we find no error in the examiner's prima facie case of obviousness as it applies to claim 11 on appeal.

For their part, appellants assert (Supplemental Brief, page 10, emphasis removed), "the issued claims in ... [Collery] are limited to use of these [gallium] compounds to treating tumors." This statement is inconsistent with the evidence of record. Not only does Collery discuss the use of gallium compositions as pharmaceutical agents having antiviral activities throughout their specification (see e.g., column 1, lines 6-10 and 39-41; column 2, lines 17-19; column 3, line 18 – column 4, line 19 and column 16, lines 5-29), Collery's claim 1 specifically states "[m]ethod for treatment of viral infections... comprising administering a gallium complex...." Accordingly, appellants' argument is not persuasive.

Appellants also assert (Supplemental Brief, bridging paragraph, page 10) that Collery's gallium compositions are "complex heterocyclic compound[s] that contain[ ], as one aspect, gallium (III) ions." In this regard, appellants assert (Supplemental Brief, page 10, emphasis removed), Collery's compositions were not "gallium per se, but compounds that contained gallium in the context of N-

heterocycles." According to appellants (Supplemental Brief, page 11), "the references do not clearly identify gallium itself as an HIV therapeutic, nor do they establish, with any reasonable probability, that if given to an HIV-infected subject, that it would have any beneficial effects in vivo." We are not persuaded by appellants' arguments for the following reasons. First, appellants' claim 11 is not limited to gallium itself, or to any particular gallium composition. In this regard, we note that the term "gallium composition" as set forth in appellants' claim 11 is open to include at least (1) gallium salts, such as gallium nitrate[3], and (2) gallium complexes, such as a gallium-hydroxypyrone complex[4]. We find nothing in appellants' specification or claims that would exclude the gallium compositions taught by Collery. In this regard, we note that appellants' reference to gallium nitrate and a gallium-hydroxypyrone complex in claims 14 and 15 respectively, serve only to broaden the scope of claim 11 to include more than these two specific compounds. Comark Communications Inc. v Harris Corp., 156 F.3d 1182, 1187, 48 USPQ2d 1001, 1005 (CAFC 1998) (it is presumed that the difference between claims is significant.). Accordingly, we are not persuaded by appellants' emphasis on Collery's teaching of gallium complexes.

Further, to the extent that appellants' assertions are suggesting that the gallium component of Collery's compositions is simply a bystander in the anti-viral activity taught by Collery, we are not persuaded. Collery teaches the anti-

[3] See e.g., appellants' specification, page 4, and claim 14, which depends from and further limits the gallium composition of claim 11 to gallium nitrate.

[4] See e.g., appellants' specification, page 4, and claim 15, which depends from and further limits the gallium composition of claim 11 to a gallium-hydroxypyrone complex.

viral activity of gallium nitrate. See e.g., Collery, column 1, lines 27-30. Collery also teaches that "preclinical toxicology tests suggest that renal and hepatic damages might be expected with gallium nitrate" as opposed to formulations of $GaCl_3$. Collery, column 1, lines 33-38. Collery then describes other gallium complexes having antiviral activity. Accordingly, to the extent that appellants' would intimate that the gallium component of Collery's compositions is simply a bystander with no anti-viral activity, we disagree.

Appellants also assert (Supplemental Brief, page 10), "there is only marginal information in ... [Collery] on the activity of these compounds, and what information there is suggest that these compounds are far less effective at inhibiting HIV (low EC_{50}/IC_{50} ratio) than existing drugs such as AZT." For the following reasons, we are not persuaded by this argument. First, to the extent that appellants assert that Collery's composition is less effective than other existing drugs, we note that "[a] known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." In re Gurley, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994). We recognize appellants' attempt to distinguish the facts on this record from those in Gurley. Reply Brief, page 7. According to appellants (id.), the question on this record "is whether the gallium compounds of the present invention would be thought useable in light of the clear indication of reduced function in ... [Collery]." We are not persuaded by appellants' argument. There is no evidence on this record to suggest that appellants' gallium composition excludes those taught by Collery. In this regard, while

appellants attempt to distinguish (Reply Brief, page 8), gallium "in and of itself" from gallium containing compositions, appellants' claim 11 is open to include gallium containing compositions as taught by Collery. Further, appellants fail to direct our attention to any evidence on this record to suggest that the gallium compositions within the scope of their claims exhibited any unexpected benefit over that taught by the combination of prior art relied upon by the examiner. In this regard, while appellants remain hesitant to acknowledge it, Collery discloses that the gallium containing compositions disclosed therein exhibit anti-viral activity.

Further, while appellants make reference to what they characterize as a "low EC_{50}/IC_{50} ratio", they make no attempt on this record to explain to what this "ratio" refers. Accordingly, we offer the following. We understand IC_{50} to refer to "the half maximal inhibitory concentration."[5] Stated differently IC_{50} represents the concentration of a drug that is required for 50% inhibition of viral replication in vitro. According to the data provided in Table VII (column 16) of Collery, all but one of the gallium compositions exhibited a higher IC_{50} than AZT. As for EC_{50}, we understand this term to refer to "the concentration of a compound that is required to obtain 50% of the maximum effect."[6] Stated differently, EC_{50} represents the plasma concentration required for obtaining 50% of the maximum effect in vivo. As seen in Collery's Table VII, a higher plasma concentration is required for the gallium compositions to obtain their maximum effect relative to

[5] See "IC50" at Wikipedia, http://en.wikipedia.org/wiki/IC50.

[6] Id. n. 5.

AZT. Collery then derives a TI based on the relationship between the IC_{50} and EC_{50} values. It is this value upon which appellants' base their arguments. As we understand it, TI refers to "therapeutic index," which is "the ratio of the toxic dose to the therapeutic dose. The therapeutic index is large when the toxic dose is much larger than the therapeutic dose."[7] As demonstrated by Collery's data, AZT has a higher TI than Collery's gallium compositions.

Nevertheless, appellants make no attempt on this record to establish that the gallium composition set forth in their claim is different from those taught by Collery. In addition, appellants make no attempt on this record to establish that their gallium compositions are unexpectedly more effective than those taught by Collery. Accordingly, we are not persuaded by appellants' arguments.

On reflection, we find no error in the examiner's prima facie case of obviousness. As discussed above, we are not persuaded by appellants' arguments to the contrary. Accordingly, we affirm the rejection of claim 11 under 35 U.S.C. § 103 as unpatentable over the combination of Narasimhan, Collery, and Bernstein. As set forth above, claims 12-30, 33, 34 and 36-40 fall together with claim 11.

Claim 31:

According to appellants (Supplemental Brief, page 11), "claim 31 contains the recitation of reducing virus shed. The examiner has not pointed to any teaching in the cited references that describes this [claim] element...." In response, the examiner finds (Answer, page 10), "the prior art discloses that

[7] See "therapeutic index," in General Practice Notebook at http://www.gpnotebook.co.uk.

gallium compositions inhibit HIV [replication], as such, one of ordinary skill in the art would expect that virus shed ... would also be reduced." We agree. Appellants provide no evidence to suggest that by inhibiting HIV replication, one would not also reduce virus shed.

Accordingly, we affirm the rejection of claim 31 under 35 U.S.C. § 103 as unpatentable over the combination of Narasimhan, Collery, and Bernstein.

Claim 32:

According to appellants (Supplemental Brief, page 12), "claim 32 recites reducing virus burden. The examiner has not pointed to any teaching in the cited references that describes this [claim] element...." In response, the examiner finds (Answer, page 10), "the prior art discloses that gallium compositions inhibit HIV [replication], as such, one of ordinary skill in the art would expect that ... viral burden would also be reduced." We agree. Appellants provide no evidence to suggest that by inhibiting HIV replication, one would not also reduce viral burden.

Accordingly, we affirm the rejection of claim 32 under 35 U.S.C. § 103 as unpatentable over the combination of Narasimhan, Collery, and Bernstein.

Claim 35:

According to appellants (Supplemental Brief, page 12), "claim 35 recites inhibiting development of AIDS. The examiner has not pointed to any teaching in the cited references that describes this [claim] element...." In response, the examiner points out that appellants acknowledge (specification, page 2) "that

infection of T-lymphocytes by HIV leads to the development of AIDS...." Answer, page 10. In addition, the examiner directs attention (Answer, page 10) to column 3 of Collery, which discloses (column 3, lines 18-61) that their "gallium (III) complexes were screened for anti-HIV-1 activity at the National Cancer Institute, ... as part of their in vitro Anti-AIDS drug Discovery Program." Accordingly, the examiner finds that "since the prior art discloses that gallium compositions inhibit HIV, one of ordinary skill in the art would expect that administration of gallium compositions would inhibit the development of AIDS." Answer, page 10. Absent evidence to the contrary, and we find none, we agree with the examiner.

Accordingly, we affirm the rejection of claim 32 under 35 U.S.C. § 103 as unpatentable over the combination of Narasimhan, Collery, and Bernstein.

Murrer and Narasimhan:

Having disposed of all claims on appeal we do not reach the merits of the rejection of claims 11-13 and 16-40 under 35 U.S.C. § 103 over the combination of Murrer, and Narasimhan.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

Joan Ellis
Administrative Patent Judge

Donald E. Adams
Administrative Patent Judge

Lora M. Green
Administrative Patent Judge

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DEA/jlb

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